

10/828,278

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S76	282	514/255.06	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/12 10:34
S77	68	S76 AND (AMILORIDE OR (SODIUM ADJ CHANNEL) OR PYRAZINOYLGUANIDINE)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/12 10:37
S78	1	("6858614").PN.	USPAT	OR	OFF	2006/12/12 10:35
S79	1	("6858615").PN.	USPAT	OR	OFF	2006/12/12 10:36
S80	1	("6903105").PN.	USPAT	OR	OFF	2006/12/12 10:36
S81	1	("7064129").PN.	USPAT	OR	OFF	2006/12/12 10:37
S82	1	("7030117").PN.	USPAT	OR	OFF	2006/12/12 10:37
S83	1	("6995160").PN.	USPAT	OR	OFF	2006/12/12 10:37
S84	1	("7026325").PN.	USPAT	OR	OFF	2006/12/12 10:37

} RELATED
PATENTS

STN SEARCH TRANSCRIPT

10/828.278

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 8 CA/SM/Capius(SM) display of CA Lexicon enhanced
NEWS 9 CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10 CAS REGISTRY(SM) updated with amino acid codes for pyrrolidine
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NEWS 16 The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 17 CHEMLIST enhanced with new search and display field
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NEWS 21 CA/Capius pre-1967 chemical substance index entries enhanced with preparation role
NEWS 22 CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 23 CA/Capius accession number crossover limit increased to 50,000
NEWS 24 CA/Capius patent kind codes will be updated
NEWS 25 CAS REGISTRY updated with new ambiguity codes
NEWS 26 CAS REGISTRY chemical nomenclature enhanced
NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V6.01C, CURRENT MACINTOSH VERSION IS V6.0C(ENG) AND V6.01C(UP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS LOGIN STN Operating Hours Plus Help Desk Availability
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=> FILE REG
COST IN U.S. DOLLARS
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ENTRY 0.21
TOTAL SESSION 0.21

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STRUCTURE FILE UPDATES: 11 DEC 2006 HIGHEST RN 915185-72-7
DICTIONARY FILE UPDATES: 11 DEC 2006 HIGHEST RN 915185-72-7

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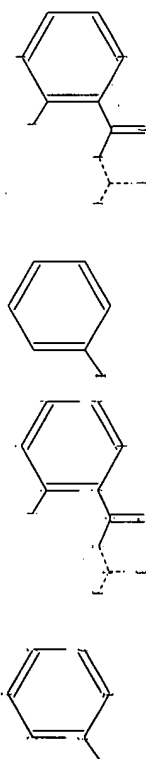
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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

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Uploading C:\Program Files\Stnexp\Queries\SODIUM CHANNEL PYRAZINE DIV METHODS.sfr



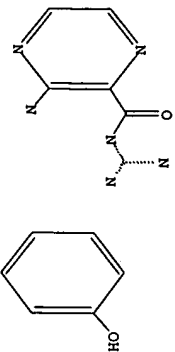
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7 9 10 11 12 13 14 21
ring nodes :
1 2 3 4 5 6 15 16 17 18 19 20
chain bonds :

5-9 6-7 9-10 9-11 11-12 12-13 12-14 19-21
 ring bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20
 exact/norm bonds :
 6-7 9-10 9-11 11-12 12-13 12-14 19-21
 exact bonds :
 5-9
 normalized bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20
 isolated ring systems :
 containing 1 : 15 :

Match level :
 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 9:CLASS 10:CLASS
 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
 20:Atom 21:CLASS

L1 STRUCTURE UPLOADED

=> d 11
 L1 HAS NO ANSWERS
 STR



Structure attributes must be viewed using STN Express query preparation.

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 SAMPLE SCREEN SEARCH COMPLETED - 55 TO ITERATE
 100.0% PROCESSED 55 ITERATIONS 0 ANSWERS
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 PROTECTED ITERATIONS: BATCH 656 TO 1544
 PROTECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s 11 sss full
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 100.0% PROCESSED 1179 ITERATIONS 26 ANSWERS
 SEARCH TIME: 00.00.01
 L3 26 SEA SSS FUL L1

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 COST IN U.S. DOLLARS
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 FILE LAST UPDATED: 11 Dec 2006 (20061211/BD)
 Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

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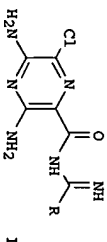
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L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER:
 DOCUMENT NUMBER:
 TITLE:

AUTHOR(S):
 Hirsch, Andrew J.; Molino, Bruce F.; Zhang, Jianzhong; Astakhova, Nadezhda; Geis, William B.; Sargent, Bruce J.; Swenson, Brian D.; Ustyalsky, Alexander; Wyle, Michael J.; Boucher, Richard C.; Smith, Rick T.; Zamurs, Andra; Johnson, M. Rose
 Parion Sciences Inc., Durham, NC, 27713, USA
 Journal of Medicinal Chemistry (2006), 49(14), 4098-4115

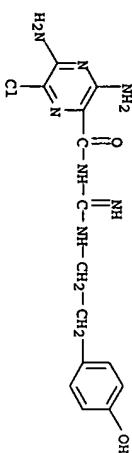
CORPORATE SOURCE:
 SOURCE:
 CODEN: JMCMAH; ISSN: 0022-2623
 American Chemical Society
 Journal
 English

PUBLISHER:
 DOCUMENT TYPE:
 LANGUAGE:
 GI



1

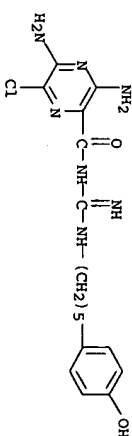
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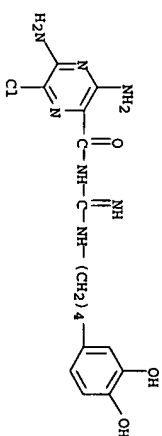
IT 583825-15-4P
 RL: PRC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (biological study); PREP (preparation); RACT (Reactant or reagent)
 (design, synthesis, and structure-activity relationships of 2-substituted pyrazinoguanidine epithelial sodium channel blockers as potential drugs for cystic fibrosis and chronic bronchitis)
 RN 583825-15-4 CAPLUS
 Pyrazineaceticboxamide, 3,5-diamino-6-chloro-N-[[[4-(4-hydroxyphenyl)butyl]amino]iminoethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Nc1nc(Cl)c(N)nc1C(=O)NCNC(=N)CCCC1=CC=C(O)C=C1

IT	583825-17-6P	583825-19-6P	583825-33-6P	
	905292-81-1P	905292-83-1P	905292-84-4P	
RL:	PAC (Pharmacological activity); SPM (Synthetic preparation); BIOL (Biological study); PREP (Preparation)			
	(design, synthesis, and structure-activity relationships of 2-substituted pyrazino[1,5-a]quinoline sodium channel blockers and chronic bronchitis)			
RN	583825-17-6	CAPUS		
	Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[15-(4-hydroxyphenyl)pentyl]amino]methoxymethyl]-, monohydrochloride (9CI)			CA
	INDEX NAME			

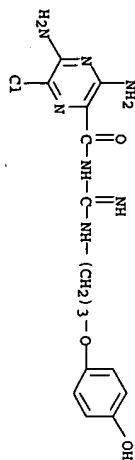


EN 563825-19-8 CAPJUS
CN Pyrazinecarboxamide, 3,5-dimino-6-chloro-N-[[4-(3,4-dihydroxyphenyl)butyl]amino]iminoethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



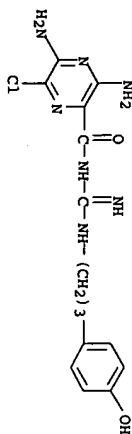
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CN	Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[3-(4	

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INDEX NAME)



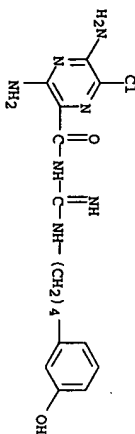
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INDEX NAME)



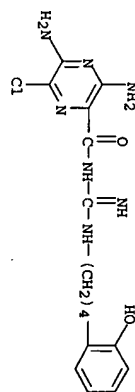
● HCl

905292-83-3 CAPLUS
Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(3-
hydroxyphenyl) butyl] amino] iminomethyl] -, monohydrochloride (9CI) (CA
INDEX NAME)



● HCl

905292-84-4 CAPLUS
Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(2-
hydroxyphenyl) butyl] amino] iminomethyl] -, monohydrochloride (9CI) (CA
INDEX NAME)



● HCl

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS ON STN
ACCESSION NUMBER: 2005:325702 CAPLUS
DOCUMENT NUMBER: 142:367646
TITLE: Methods using sodium channel blockers for reducing
risk of infection from pathogens
INVENTOR(S): Johnson, Michael R.; Hopkins, Samuel E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 52 pp.
DOCUMENT TYPE: CODEN: USXXCO
LANGUAGE: Patent
FAMILY ACC. NUM. COUNT: 1 English
PATENT INFORMATION:

RCI. MPN

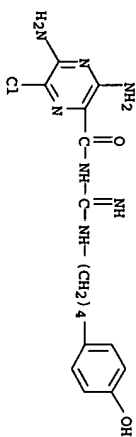
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005080093	A1	20050414	US 2004-920484	20040818
AU 2004287352	A1	20050519	AU 2004-287352	20040819
CA 2534069	AA	20050519	CA 2004-2534069	20040819
WO 2005044180	A2	20050519	WO 2004-US26778	20040819
WO 2005044180	A3	20051006		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GR, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, ST, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, RW, BM, GH, GM, KE, LS, MW, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, HT, IL, MR, NE, SN, TD, TG	A2	20060517	RP 2004-816810	20040819
EP 1656022				
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PRIORITY APPLN. INFO.:				
US 2003-496482P	P	20030820		
US 2004-920484	A	20040818		
WO 2004-US26778	W	20040819		

OTHER SOURCE(S): MARPAT 142:367646
AB Prophylactic treatment methods are provided for protection of individuals and/or populations against infection from airborne pathogens. In particular, prophylactic treatment methods are provided comprising administering a sodium channel blocker or pharmaceutically acceptable salt thereof to one or more members of a population at risk of exposure to or already exposed to one or more airborne pathogens, either from natural sources or from intentional release of pathogens into the environment.
IT 563825-14-3 563825-15-4 563825-16-5

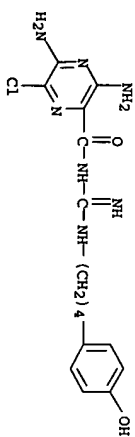
583825-18-7 583825-23-4 583825-25-6
849588-70-1 849588-71-2 849588-72-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

583825-14-3 CAPLUS
(sodium channel blockers for reducing risk of infection from pathogens)
RN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(4-
CN hydroxyphenyl)butyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)

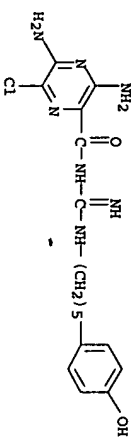


RN 583825-15-4 CAPLUS
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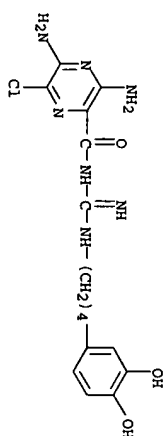


● HCl

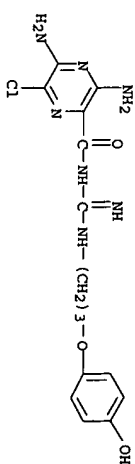
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hydroxyphenyl)pentyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



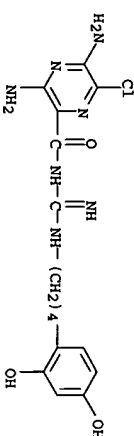
RN 583825-18-7 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(3,4-
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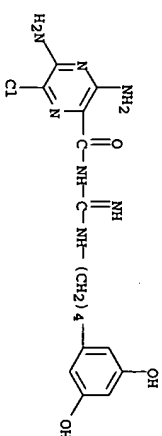
RN 583825-23-4 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[13-(4-
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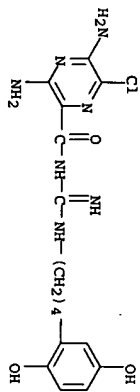
RN 583825-25-6 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(2,4-
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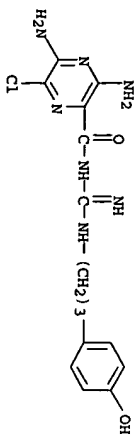
RN 849588-70-1 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(3,5-
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RN 849588-71-2 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(2,5-
dihydroxyphenyl)butyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



RN 849588-72-3 CAPLUS
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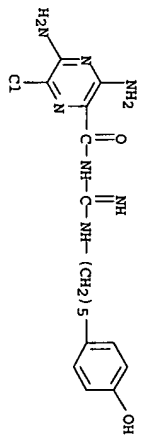


L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:678615 CAPLUS
DOCUMENT NUMBER: 139:191482
TITLE: Sodium channel blockers
INVENTOR(S): Johnson, Michael R.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXX2D
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

APPLICATION

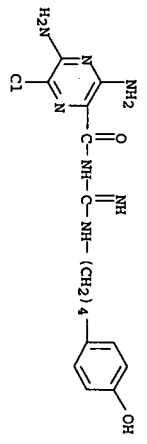
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070184	A2	20030828	WO 2003-US4823	20030219
WO 2003070184	A3	20040617		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: CH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GT, HT, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
US 2003195160	A1	20031016	US 2002-76551	20020219
US 6838614	B2	20050222		
CA 2476837	AA	20030828	CA 2003-2476837	20030219
AU 2003215286	A1	20030909	AU 2003-215286	20030219
EP 1485359	A2	20041215	EP 2003-711105	20030219
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JP 2005526726	T3	20050908	JP 2003-569144	20030219
US 2004198744	A1	20041007	US 2004-828278	20040421
US 2004198745	A1	20041007	US 2004-828278	20040421
US 2004198746	A1	20041007	US 2004-828353	20040421

US 2004198747 A1 20041007 US 2004-828354 20040421
US 2004204424 A1 20041014 US 2004-828235 20040421
PRIORITY APPLN. INFO.: WO 2003-US4823 W 20030219
OTHER SOURCE(S): MARPAT 139:191482
AB The present invention relates to sodium channel blockers (Markush structures are included). The present invention also includes a variety of methods of treatment using these novel sodium channel blockers.
IT 583825-17-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RN 583825-17-6 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-((15-(4-hydroxyphenyl)pentyl)amino)iminomethyl)-(9CI) (CA INDEX NAME)

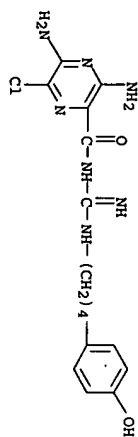


IT 583825-14-3P 583825-15-4P 583825-16-5P
583825-18-7P 583825-19-8P 583825-23-4P
583825-24-5P 583825-25-6P 583825-26-7P
583825-33-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Sodium channel blockers for therapy of pulmonary and other diseases)

RN 583825-14-3 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-((14-(4-hydroxyphenyl)butyl)amino)iminomethyl)-(9CI) (CA INDEX NAME)

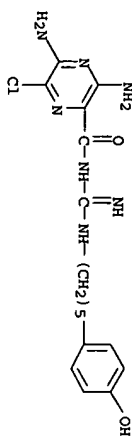


RN 583825-15-4 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-((14-(4-hydroxyphenyl)butyl)amino)iminomethyl)-(9CI) (CA INDEX NAME)

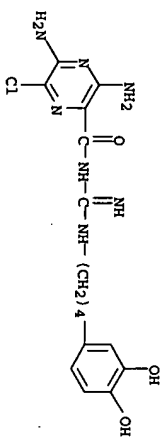


● HCl

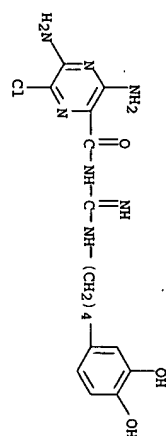
RN 583825-16-5 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[5-(4-hydroxyphenyl)pentyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



RN 583825-18-7 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(3,4-dihydroxyphenyl)butyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)

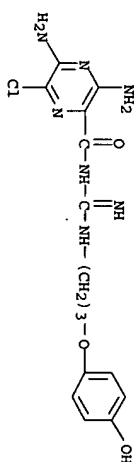


RN 583825-19-8 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(3,4-dihydroxyphenyl)butyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

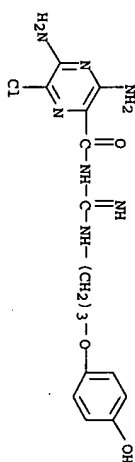


● HCl

RN 583825-23-4 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[3-(4-hydroxyphenoxy)propyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)

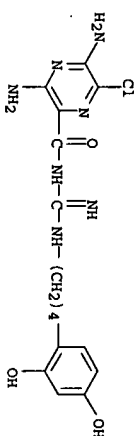


RN 583825-24-5 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[3-(4-hydroxyphenoxy)propyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

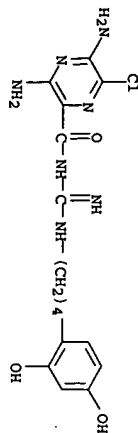


● HCl

RN 583825-25-6 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(2,4-dihydroxyphenyl)butyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)

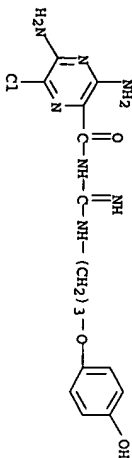


RN 583825-26-7 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[(1-(4-(2,4-dihydroxyphenyl)butyl)amino)iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 583825-33-6 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[(1-(3-(4-hydroxyphenoxy)propyl)amino)iminomethyl]-, monohydrobromide (9CI) (CA INDEX NAME)

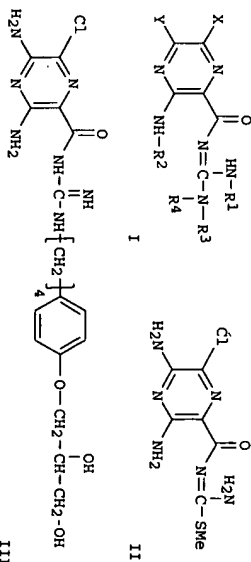


● HBr

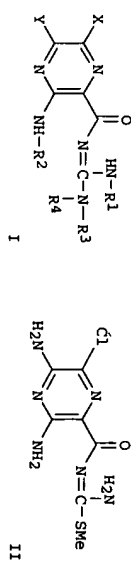
L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:678613 CAPLUS
DOCUMENT NUMBER: 139:214488
TITLE: Preparation of diaminopyrazines as sodium channel blockers for promoting the hydration of mucosal surfaces
INVENTOR(S): Johnson, Michael R.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 139 pp.
DOCUMENT TYPE: CODEN: PIXXD
LANGUAGE: Patent
FAMILY ACC. NOM. COUNT: 1 English
PATENT INFORMATION: RELATED APP'N.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070182	A2	20030828	WO 2003-US4817	20030219
WO 2003070182	A3	20031224		
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US 2003199456 A1 20031023 US 2002-76571 20020219
US 6858615 B2 20050222
CA 2476430 AA 20030828 CA 2003-2476430 20030219
AU 200321135 A1 20030509 AU 2003-21135 20030219
EP 1485360 A2 20041215 EP 2003-742810 20030219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, AL, TR, BG, CZ, EE, HU, SK, JP 2005530692 T2 20051013 JP 2003-569142 20030219
US 2004198748 A1 20041007 US 2004-828466 20040421
US 2004198749 A1 20041007 US 2004-828479 20040421
US 2004204425 A1 20041014 US 2004-828352 20040421
US 2004229884 A1 20041118 US 2004-828171 20040421
US 2006142306 A1 20060629 US 2005-532110 20050421
PRIORITY APPL. INFO.: US 2002-76571 20020219
OTHER SOURCE(S): MANPAT 139:214488 WO 2003-US4817 A 20030219
G1



III

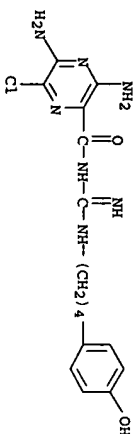


II

AB Title compds. I [X = H, halo, CF3, etc.; Y = H, OH, SH, etc.; R1 = H, alkyl; R2 = R7, (CH2)mOR8, (CH2)mNR9R10, etc.; R3, R4 = H, alkyl, hydroxyalkyl, etc. with provisos; R7 = H, alkyl; R8 = H, alkyl, glucuronide, etc.; R10 = H, SO2CH3, CO2R7, etc.; m = 1-7] and their pharmaceutically acceptable salts were prepared. For example, condensation of thiourea II hydroiodide and 4-[(2,3-dihydroxypropyl)oxy]phenylbutylamine e, e.g., prepared from 4-(4-hydroxyphenyl)butylamine in 4-steps, afforded diaminopyrazine III hydrochloride in 53% yield. In canine bronchial epithelial sodium channel blocking activity assays, 12-examples of compds. I exhibited fold-enhancement values relative to amiloride ranging from 11.2-124, e.g., the fold-enhancement value of diaminopyrazine III hydrochloride was 124. Compds. I are claimed useful as antidiarrhetics, laxatives, antihypertensives, etc.

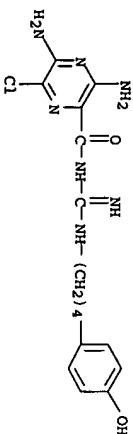
IT 583825-15-4p
RU: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USRS (Uses)
(drug candidate; preparation of mucosal surfaces)
for promoting the hydration of mucosal surfaces
RN 583825-15-4 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[(1-(4-(4-hydroxyphenyl)butyl)amino)iminomethyl]-, monohydrochloride (9CI) (CA

INDEX NAME)



● HCl

IT 583825-14-3P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOD (Biological study); PREP (Preparation); USSES (Uses)
 (drug candidate; preparation of diamino pyrazines as sodium channel blockers for promoting the hydration of mucosal surfaces)
 RN 583825-14-3 CAPLUS
 CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[(4-(4-hydroxyphenyl)butyl)amino]iminomethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS ON STN
 ACCESSION NUMBER: 1992:605669 CAPLUS
 DOCUMENT NUMBER: 117:205669
 TITLE: Novel amiloride analog allosterically modulates the α_2 -adrenergic receptor but does not inhibit sodium/hydrogen ion exchange

AUTHOR(S): Wilson, Amy L.; Womble, Scott N.; Prakash, Chandra; Cragoe, E. J., Jr.; Blair, Ian A.; Limbird, Lee E. Sch. Med., Vanderbilt Univ., Nashville, TN, 37332-6600, USA

CORPORATE SOURCE: Molecular Pharmacology (1992), 42(2), 175-9

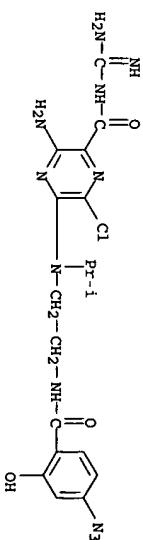
SOURCE: CODEN: MOPMAJ; ISSN: 0026-895X

DOCUMENT TYPE: Journal

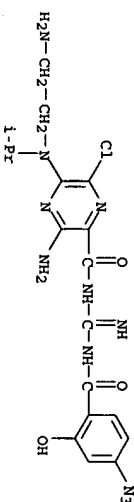
English

AB Two novel amiloride analogs have been synthesized during the course of efforts to develop a photoaffinity label for the amiloride allosteric domain on α_2 -adrenergic receptors. One of these, 5-(N-2'-aminoethyl-N'-isopropyl)amiloride-N-[4"-azidosalicylamide] (A-EIA-AS), markedly accelerates the rate of dissociation of [³H]yohimbine from affinity-purified α_2 -adrenergic receptors, an assay for allosteric modulation of receptor-adrenergic ligand interactions. In contrast, this agent does not appreciably inhibit Na⁺/H⁺ exchange, measured as 5-(N-ethyl-N-isopropyl)amiloride (EIA)-inhibitable 22Na⁺ uptake into cultured renal epithelial cells. A second analog, 5-(N'-2'-(4"-azidosalicylamido)ethyl-N'-isopropyl)amiloride (ASA-EIA), does not foster an accelerated rate of dissociation of [³H]yohimbine binding

from the α_2 receptor but does block the ability of A-EIA-AS to do so, suggesting that ASA-EIA and A-EIA-AS interact at a common binding site. Interestingly, the ability of EIA to accelerate [³H]yohimbine dissociation is not blocked by ASA-EIA, a finding that may indicate that EIA and A-EIA-AS allosterically modulate α_2 receptor-ligand interactions via distinct or nonoverlapping binding sites.
 IT 144176-47-6 144176-48-7
 RL: BIOD (Biological study)
 (adrenergic receptor modulation by, hydrogen ion-sodium exchange in relation to)
 RN 144176-47-6 CAPLUS
 CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[(2-[(4-azido-2-hydroxybenzoyl)amino]ethyl) (1-methylethyl)amino]-6-chloro- (9CI) (CA INDEX NAME)



RN 144176-48-7 CAPLUS
 CN Pyrazinecarboxamide, 3-amino-5-[(2-aminoethyl) (1-methylethyl)amino]-N-[(4-azido-2-hydroxybenzoyl)amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS ON STN
 ACCESSION NUMBER: 1991:441425 CAPLUS
 DOCUMENT NUMBER: 115:41425
 TITLE: Reversal of intrinsic multidrug resistance in Chinese hamster ovary cells by amiloride analogs

AUTHOR(S): Eppard, R. F.; Eppard, R. M.; Gupta, R. S.; Cragoe, E. J., Jr. Health Sci. Cent., McMaster Univ., Hamilton, ON, L8N 3Z5, Can.

CORPORATE SOURCE: British Journal of Cancer (1991), 63(2), 247-51

SOURCE: CODEN: BJCAAI; ISSN: 0007-0920

DOCUMENT TYPE: Journal

English

AB A number of amiloride analogs can sensitize wild type Chinese hamster ovary (CHO) cells to the cytotoxic action of vinblastine, daunomycin, puromycin or colchicine. Some of these analogs also have weak sensitizing effects on the multidrug resistant CHO cell line, CHRC5. The unusual feature of most of the active amiloride analogs is that they are more potent in reversing the intrinsic multidrug resistance (MDR) phenotype of CHO cells than their acquired MDR characteristic. Human HeLa cells that do not exhibit intrinsic MDR are not affected by these agents. Several of the amiloride analogs have a greater effect in increasing adriamycin uptake in wild type CHO cells than they do with CHRC5 cells. The differential

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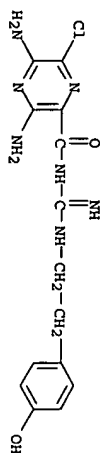
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10/228, 218
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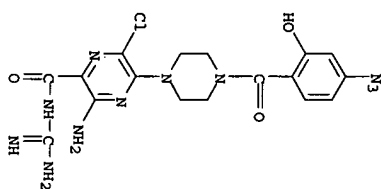
effect of amiloride analogs on intrinsic vs. acquired MDR characteristics of Chinese hamster cells suggests some differences in the underlying resistance mechanisms.

IT 134788-24-2
 RL: BIOL (Biological study)
 (multiple resistance to neoplasm inhibitors inhibition by)
 RN 134788-24-2 CAPLUS
 CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[2-(4-hydroxyphenyl)ethyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)

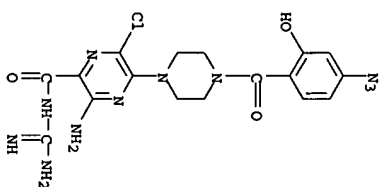


LA ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS ON STN
 ACCESSION NUMBER: 1990/402710 CAPLUS
 DOCUMENT NUMBER: 113:2710
 TITLE: Photoactivatable probe for the sodium/hydrogen ion exchanger cross-links a 66-kDa renal brush border membrane protein
 AUTHOR(S): Ross, Willie; Bertrand, William; Morrison, Aubrey
 CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA
 SOURCE: Journal of Biological Chemistry (1990), 265(10), 5341-4
 CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Earlier studies on LLC-PK1 cells have demonstrated 2 pharmacol. distinct Na+/H+ exchangers in renal epithelia. In addition, the cDNA clone for the human Na+/H+ antiporter which is growth factor activatable has been isolated and expressed (Sardet, C., et al., 1989). Here the synthesis of an amiloride analog that can be photoactivated and labeled with 125I is reported. This analog covalently crosslinks a 66-kDa protein of bovine renal brush border membranes. A rabbit polyclonal antibody that was directed against a 20-amino acid peptide of the cytoplasmic domain of its human Na+/H+ antiporter also gives a pos. Western against 66-kDa protein of bovine brush border membranes. Thus, the photoactive probe may be helpful in the isolation and purification of the brush border Na+/H+ exchanger.
 IT 127628-92-6P
 RL: SPN (Synthetic preparation); PRP (Preparation)
 (preparation and radioiodination of)
 RN 127628-92-6 CAPLUS
 CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[4-(4-azido-2-hydroxybenzoyl)-1-piperazinyl]-6-chloro- (9CI) (CA INDEX NAME)



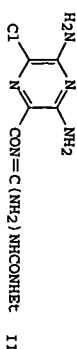
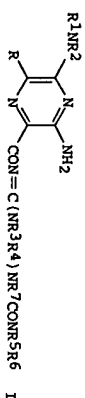
IT 127513-40-0P
 RL: PRP (Preparation)
 (preparation of, as photoactivatable probe for sodium-hydroxy ion exchanger)
 RN 127513-40-0 CAPLUS
 CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[4-(4-azido-2-hydroxy-3(or 5)-(iodo-125I)benzoyl)-1-piperazinyl]-6-chloro- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:509585 CAPLUS
DOCUMENT NUMBER: 89:109585
TITLE: Pyrazinecarboxamides
INVENTOR(S): Cragoe, Edward J., Jr.; Woltersdorf, Otto W., Jr.;
Habecker, Charles N.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 15 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

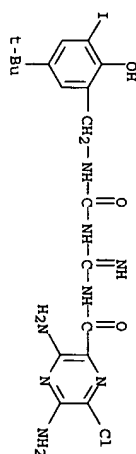
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US 4085211	A	19780418	US 1976-722442	19760913
DK 7605314	A	19770616	DK 1976-5314	19761125
SE 7613289	A	19770616	SE 1976-13289	19761126
SE 431452	B	19840206		
SE 431452	C	19840517		
NL 7613276	A	19770617	NL 1976-13276	19761129
AU 7620181	A1	19780608	AU 1976-20181	19761202
AU 511429	B2	19800821		
ES 454160	A1	19780301	ES 1976-454160	19761210
FR 2335226	A1	19770715	FR 1976-37459	19761213
FR 2335226	B1	19790309		
GB 1527297	A	19781004	GB 1976-51940	19761213
HU 175504	P	19800828	HU 1976-ME2034	19761213
CH 630369	A	19820615	CH 1976-15660	19761213
BE 849379	A1	19770614	BE 1976-173235	19761214
ZA 7607431	A	19780726	ZA 1976-7431	19761214
JP 52106877	A2	19770907	JP 1976-149889	19761215
JP 62038350	B4	19870817		
ES 465742	A1	19781001	ES 1978-465742	19780103
			US 1975-640803	A2 19751215

PRIORITY APPLN. INFO.: MARPAT 89:109585
OTHER SOURCE(S):
GI



AB A series of title amides I (R = halo, R1 = H, alkyl, cycloalkyl, alkenyl;
R2 = H, alkyl, NR1R2 = pyrrolidino, piperidino; R3 = H, alkyl, cycloalkyl;
R4 = H, alkyl, cycloalkyl; R5 = H, alkyl, cycloalkyl, Ph, substituted
phenyl; R6 = H, alkyl, cycloalkyl; RSR6 = morpholino, piperazino; R7 = H,
alkyl; R3R7 = CH2CH2, substituted ethylene) were prepared and are useful as
diuretics (no data). Thus, the addition reaction of N-amidino-3,5-diamino-6-
chloro-2-pyrazinecarboxamide with EtNCO gave II.
IT 64077-96-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
RN 64077-96-9 CAPLUS

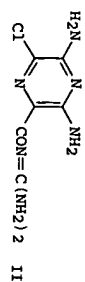
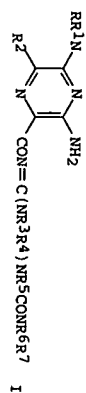
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[(1,1-dimethylethyl)-2-
hydroxy-3-iodophenyl]methyl]amino]carbonyl]amino]iminoethyl]- (9CI) (CA
INDEX NAME)



L4 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:517906 CAPLUS
DOCUMENT NUMBER: 87:117906
TITLE: Pyrazinecarboxamides
INVENTOR(S): Cragoe, Edward J., Jr.; Woltersdorf, Otto William,
Jr.; Habecker, Charles Newcomer
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Ger. Offen., 71 pp.
CODEN: GXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2656374	A1	19770616	DE 1976-2656374	19761213
DE 2656374	C2	19890810		
DK 7605314	A	19770616	DK 1976-5314	19761125
SE 7613289	A	19770616	SE 1976-13289	19761126
SE 431452	B	19840206		
SE 431452	C	19840517		
NL 7613276	A	19770617	NL 1976-13276	19761129
AU 7620181	A1	19780608	AU 1976-20181	19761202
AU 511429	B2	19800821		
ES 454160	A1	19780301	ES 1976-454160	19761210
FR 2335226	A1	19770715	FR 1976-37459	19761213
FR 2335226	B1	19790309		
GB 1527297	A	19781004	GB 1976-51940	19761213
HU 175504	P	19800828	HU 1976-ME2034	19761213
CH 630369	A	19820615	CH 1976-15660	19761213
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ZA 7607431	A	19780726	ZA 1976-7431	19761214
JP 52106877	A2	19770907	JP 1976-149889	19761215
JP 62038350	B4	19870817		
ES 465742	A1	19781001	ES 1978-465742	19780103
			US 1975-640803	A 19751215

PRIORITY APPLN. INFO.:
GI



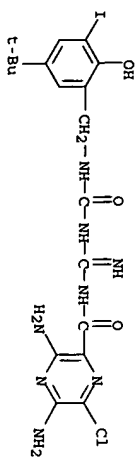
AB Diuretic (no data) pyrazinecarboxamides I (R, R₁, R₃, R₄, R₅, R₇ = H, alkyl; R₂ = halo; R₆ = H, alkyl, aryl) (>60 compds.) were prepared. Thus II was treated with PIVCO to give I (R, R₁, R₃, R₄, R₅, R₇ = H, R₂ = Cl, R₆ = Pr).

IT 64077-96-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 64077-96-9 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[[(5-(1,1-dimethylethyl)-2-hydroxy-3-iodophenyl)methyl]amino]carbonyl]amino]iminoethyl] - (9CI) (CA INDEX NAME)



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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD: